UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/628,494	07/28/2000	Emmanuel Mignot	HPZ-017	3784

7590 08/28/2002

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109

EXAMINER
SOUAYA, JEHANNE E

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/28/2002

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/628,494	Applicant(s) MIGNOT, EMMANUEL	
	Examiner Jehanne Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-12 and 38-45* is/are pending in the application.

4a) Of the above claim(s) *38-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-12 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *2* .

DETAILED ACTION

Election/Restriction

1. Claims 38-44 are withdrawn from further consideration as being drawn to a nonelected invention. Election was made without traverse in Paper No. 14. An action on the merits of claims 1-3, 5-12 and 45 follows.

Claim Rejections - 35 USC § 112

2. Claims 1-3, 5-12, and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining a predisposition to narcolepsy in canines by detecting a deletion of exon 4 or exon 6 of the hypocretin 2 receptor or to a method for determining a predisposition to narcolepsy in humans by detecting decreased levels of hypocretin 1 ligand as compared to the level of hyopcretin 1 in a normal control, does not reasonably provide enablement for detecting a predisposition to any disorder in any subject caused by any alteration in hypocretin receptor activity by analyzing nucleic acid from a subject to detect the presence of at least one polymorphism that predisposes the subject to a disorder caused by an alteration in activity of any hypocretin receptor, or methods dependant therefrom wherein the disorder is any sleep disorder or any sleep disorder that is characterized by increased wakefulness or decreased wakefulness, or wherein the disorder is any mood disorder, chronic fatigue syndrome, or attention deficit disorder, or wherein the individual is human or canine, or detecting any polymorphism within a genomic region between markers 26-8 and 530-3 of canine

chromosome 12, or any truncated HCRtr2 transcript. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to detecting a predisposition to any disorder in any subject (encompasses any species) caused by any alteration in hypocretin receptor activity by analyzing nucleic acid from a subject to detect the presence of at least one polymorphism that predisposes the subject to a disorder caused by an alteration in activity of a hypocretin receptor. The claims are further broadly drawn to detecting any sleep disorder or mood disorder, chronic fatigue syndrome, or attention deficit disorder. The claims are also broadly drawn to detecting a polymorphsims that is anywhere between markers 26-8 and 530-3 and wherein the polymorphism is any truncated HCRtr2 transcript. The specification defines "polymorphism" to refer to a marker that is distinguishably different as compared to an analogous region from a subject of the same species (p. 13), thus the term encompasses deletions and insertions, as well as single nucleotide polymorphisms. The specification further defines "hypocretin-related disorder" and "disorder caused by an alteration in hypocretin receptor activity" as a disorder that is caused by an increase or decrease in binding of hypocretin relative to that found in an unaffected subject. Further the specification asserts that an increase or decrease in hypocretin receptor activity can be caused by increased or decreased levels or availability of hypocretin ligand, alterations in a hypocretin receptor that affect the binding affinity of the receptor for hypocretin, and alterations in the hypocretin polypeptide that affect its binding affinity to a hypocretin receptor (p 11).

Therefore the claims broadly encompass any mutation or polymorphism, which encompasses polymorphisms in coding as well as non coding sequences that are not limited to genomic or cDNA for hypocretin or hypocretin receptor, but include any sequences that affect regulation of such, that affects either the level of hypocretin peptide or hypocretin receptor or the binding affinity of one to the other.

While the claims broadly encompass any disorder, any sleep disorder, any sleep disorder characterized by increased or decreased wakefulness, or any mood disorder, chronic fatigue syndrome or attention deficit disorder, the specification has only taught that deletions in exon 4 or exon 6 in the hypocretin 2 receptor (pp 53, and 55 of the specification) is associated with narcolepsy in canines while a decreased level of hypocretin 1 ligand is associated with narcolepsy in humans. The specification provides no working examples that either the mutations in hypocretin receptor 2 or decreased levels of hypocretin 1 ligand is associated with any other disorder, such as any sleep disorder characterized by increased or decreased wakefulness or any mood disorder, chronic fatigue syndrome, or attention deficit disorder. Further, Aldrich (Neurology, vol. 50 suppl, pp s2-s7, 1998) teaches that while sleepiness can be a useful though not a definitive diagnostic tool, sleepiness, defined as a propensity to fall asleep easily in relaxed or sedentary situation, occurs mainly in sleep disorders and must be distinguished from fatigue and tiredness, which denote a lack of energy, motivation, or strength and which may occur with sleep disorders as well as with a variety of systemic and psychiatric disorders (see p. S2, col. 2, last para). Aldrich further teaches that daytime sleep attacks, which are episodes of daytime

sleep that occur without warning, are not specific for narcolepsy and that they may occur in association with any disorder that leads to severe chronic sleepiness (p. S3, col 1, 1st full para). Therefore, while sleep disorders (such as sleep apnea, or idiopathic hyperinsomnia), mood disorder, chronic fatigue syndrome, or attention deficit disorder, may share a common symptom with narcolepsy, neither the specification nor the art teach an association between any polymorphism in either of the hypocretin receptors or hypocretin levels and these disorders. Further, neither the specification or the art provide any teaching of the affect of either the polymorphisms in hypocretin receptor 2 or decreased levels of hypocretin 1 on any of the symptoms of narcolepsy, nor how these aberrant mutations or levels cause narcolepsy such that the skilled artisan would be able to establish a predictable correlation that the association of narcolepsy with the aberrant mutations or levels taught in the specification are also associated with sleep apnea, idiopathic hyperinsomnia, mood disorder, chronic fatigue syndrome, or attention deficit disorder. These disorders, especially the broadly stated "sleep disorder" and "mood disorder" represent heterogenous disorders whose causes are not well understood and whose association to narcolepsy is also unknown. To practice the invention as broadly as it is claimed the skilled artisan would have to perform a study which included a large number of different disorders, including different types of sleep disorders, mood disorders, chronic fatigue syndrome, and attention deficit disorder, screen subjects with these disorders as well as controls for any mutation in any hypocretin receptor or any aberrant levels of either hypocretin receptors or ligands to determine if polymorphisms that affect hypocretin receptor activity are associated

with these disorders. Because neither the specification nor the art provide any predictable correlation between mutations or polymorphisms which affect hypocretin receptor activity and any disorder, such a study would require mainly trial and error analysis the results of which are unpredictable. The claims also broadly encompass any polymorphism that affects hypocretin receptor activity, however the specification has only taught that deletions in exon 4 or exon 6 in the hypocretin 2 receptor (pp 53, and 55 of the specification) is associated with narcolepsy in canines while a decreased level of hypocretin 1 ligand is associated with narcolepsy in humans (p. 56). These aberrations are not predictably representative of the large number of polymorphisms encompassed by the claimed invention. While the deletions of exon 4 and exon 6 in hypocretin receptor 2 are associates with narcolepsy in canines, it is unclear from the teachings in the specification how these mutations affect hypocretin receptor activity such that narcolepsy results. The specification teaches that a large number of polymorphsims in hypocretin as well as hypocretin receptors 1 and 2 in humans were screened for an association with narcolepsy, but that none was found (p 61). Therefore, to practice the invention as broadly as it is claimed, the skilled artisan would have to screen both canine and human hypocretin receptors (hypocretin 1 and hypocretin 2) and hypocretin ligands to be able to determine which mutations were correlated with narcolepsy, or any disorder. As the specification teaches that a large number of polymorphisms, which includes polymorphisms that resulted in codon changes, were not associated with narcolepsy, such an analysis would require trial and error

manipulations, the results of which are clearly unpredictable as exemplified by the teachings in the specification. Such analysis is therefore considered undue.

Conclusion

3. No claims are allowable.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
Art Unit 1634
August 22, 2002